REMARKS

Claims 41-66 are pending in this application. Currently claims 41, 42, 45 and 46 are under consideration by the Examiner for prosecution purposes of this application. By this Amendment, claim 41 has been amended and the remaining claims are unchanged..

Claim 41 has been amended in the interest of expediting prosecution, i.e., to obviate the § 112, first paragraph (written description and enablement) rejections, and not for reasons related to patentability. Claim 41 b) has been amended to include that the claimed polypeptide that is at least "90%" identical to the amino acid sequence of SEQ ID NO:1 has "extracellular matrix protein activity". Support for this amendment can be found throughout the specification, for example, at page 17, lines 3-6 and page 54, line 14 to page 55, line 1. Claim 41 c) has been amended to include that the claimed biologically active fragment has "extracellular matrix protein activity". Support for this amendment can be found throughout the specification, for example at page 54, line 14 to page 55, line 1. Claim 41 (d) has been amended to include that the claimed immunogenic fragment consists "of at least 5 amino acids" of the amino acid sequence of SEQ ID NO:1. Support for this amendment can be found throughout the specification, for example at page 8, lines 25 and 26.

Rejoinder of Claims

Applicants continue to request the rejoinder of claims 43, 44 and 47-50 directed to methods of producing the claimed polypeptides and of using the claimed polypeptides upon allowance of a product claim per the Commissioner's Notice in the Official Gazette of March 26, 1996, entitled "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103 (b)" which sets forth the rules, upon allowance of product claims, for the rejoinder of process claims covering the same scope of products.

Rejection under 35 U.S.C. §112, first paragraph (written description)

Claims 41 and 45 stand rejected under the first paragraph of 35 U.S.C. §112 for allegedly containing subject matter "not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed,

had possession of the claimed invention" for the reasons asserted at pages 2-4 of the August 19, 2002 Office Action.

A. Legal Requirements

> . . . the applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the "written description" inquiry, *whatever is now claimed. Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991)

Attention is also drawn to the Patent and Trademark Office's own "Guidelines for Examination of Patent Applications Under the 35 U.S.C. Sec. 112, para. 1", published January 5, 2001, which provide that:

> An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics[42] which provide evidence that applicant was in possession of the claimed invention,[43] i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.[44] What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail.[45] If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met.[46][footnotes are omitted]

Thus, the written description standard is fulfilled by both what is specifically disclosed and what is conventional or well known to one skilled in the art.

B. The Specification provides an adequate written description of the claimed "variants" of SEQ ID NO:1.

The subject matter recited in amended claim 41 is adequately disclosed in the Specification given what is are conventional or well known to one skilled in the art.

Please note that the "variant" language of independent claim 41 has been amended to claim "a polypeptide comprising an amino acid sequence at least **90%** identical to the amino acid sequence of SEQ ID NO:1, **said polypeptide having extracellular matrix protein activity** [emphasis added]". It is submitted that the Specification provides an adequate written

description of the claimed variants of SEQ ID NO:1 to convey with reasonable clarity to those skilled in the art that applicants were in possession of the invention as "now" claimed at the time of the filing of this application.

Variants of SEQ ID NO:1 are defined in the Specification at, for example, at page 17, lines 3-6. Polypeptide sequence variants are know by one of skill in the art to have amino acid substitutions which do not alter the function of the polypeptide. For example, a change of an amino acid residue to another at the extreme amino- or the carboxy-terminus of the sequence most likely will not alter the function of the polypeptide. The Specification defines specific structural domains related to extracellular matrix proteins at page 15, line 17 to page 16, line 2, and specifically to the S1-5 protein at page 16, lines 3-6 and Figure 3.

In addition, attached is the Nakamura, T. *et al.* reference that corroborates applicants' assertion that the claimed polypeptide having the amino acid sequence of SEQ ID NO:1 is related to the S1-5 protein. In this reference, ECMP-1 is referred to as "DANCE" and the abstract states that "DANCE and recently described protein S1-5 comprise a new EGF-like protein family." This reference also teaches that DANCE is a novel ligand for integrin receptors and may play a role in vascular development and remodeling.

Accordingly, for all the above reasons, it is well within the skill of those in this art to identity those polypeptides comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1 and that these polypeptide variants retain the extracellular matrix protein activity.

Furthermore, an assay to measure extracellular matrix protein activity is defined in the Specification at page 54, Example X. Assays to determine functional activity are considered routine experimentation when identifying functional sequence variants. One of ordinary skill in the art would recognize polypeptide sequences which are variants having at least 90-99% amino acid identity to SEQ ID NO:1, as those polypeptide sequences which, when assayed, have extracellular matrix protein activity. Thus, polypeptides comprising an amino acid sequence that is 90-99% identical to the amino acid sequence of SEQ ID NO:1 can easily be identified by one of skill in the art based on both the presence of functional and structural domains and by the assay all disclosed in the Specification. Accordingly, Applicants have disclosed the claimed invention

in sufficient detail and provided identifying characteristics such that the skilled artisan would understand that Applicants were in possession of the claimed invention.

Thus, the Specification provides an adequate written description of the claimed variants of SEQ ID NO:1 to convey with reasonable clarity to those skilled in the art that applicants were in possession of the invention as "now" claimed at the time of the filing of this application. Therefore, reconsideration and withdrawal of this rejection to the claims are respectfully requested.

Rejection under 35 U.S.C. §112, first paragraph (enablement)

Claims 41 and 45 stand rejected under the first paragraph of 35 U.S.C. §112 because allegedly the Specification does not reasonably provide enablement for biologically active or immunogenic fragments of SEQ ID NO:1 or naturally-occurring sequences with at least 85% identity to SEQ ID NO:1 for the reasons asserted at pages 4-6 of the August 19, 2002 Office Action.

To fulfill the enablement requirement of 35 U.S.C. §112, first paragraph, the claimed invention must be described in the specification in such as way as to enable one skilled in the relevant art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. It is submitted that the Specification does reasonably provide an adequate written description to **enable** the variants, biologically active and immunogenic fragments of SEQ ID NO:1 as "now" claimed at the time of the filing of this application.

The Examiner is well aware that relative skill of those in the art is very high and the amount of direction or guidance needed to be disclosed in the Specification to make the variants, biologically active and immunogenic fragments of SEQ ID NO:1 as "now" claimed. As mentioned above, the claimed variants of SEQ ID NO:1 are defined in the Specification at, for example, at page 17, lines 3-6. Polypeptide sequence variants are know by one of skill in the art to have amino acid substitutions which do not alter the function of the polypeptide. For example, a change of an amino acid residue to another at the extreme amino- or the carboxy-terminus of the sequence most likely will not alter the function of the polypeptide. The Specification defines specific structural domains related to extracellular matrix proteins at page 15, line 17 to page 16, line 2, and specifically to the S1-5 protein at page 16, lines 3-6 and Figure 3. In addition,

attached is the Nakamura, T. *et al.* reference that corroborates applicants' assertion that the claimed polypeptide having the amino acid sequence of SEQ ID NO:1 is related to the S1-5 protein.

Furthermore, the claimed variants and biologically active fragments of SEQ ID NO:1 could be simply assayed for extracellular matrix protein activity (*see* page 54 of Specification, Example X). Assays to determine functional activity are considered routine experimentation when identifying functional sequence variants. One of ordinary skill in the art would recognize polypeptide sequences which are variants having at least 90-99% amino acid identity to SEQ ID NO:1 or biologically active fragments of SEQ ID NO:1, as those polypeptides or fragments which, when assayed, have extracellular matrix protein activity. Accordingly, polypeptides comprising an amino acid sequence that is 90-99% identical to the amino acid sequence of SEQ ID NO:1 or biologically active fragments of SEQ ID NO:1 can easily be identified by one of skill in the art based on both the presence of functional and structural domains and by the assay all disclosed in the Specification.

Similarly, the immunogenic fragment of the claimed polypeptide is described in the specification in such as way as to enable one skilled in the relevant art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The Specification, at page 8, lines 25 and 26, teaches that the immunogenic fragments of ECMP are preferably about 5 to about 15 amino acids in length. Furthermore, at page 55, Example XI, the Specification specifically teaches how to produce ECMP-1 specific antibodies. This approach is confirmed in the Nakamura, T. *et al.* reference, which made antibodies to DANCE using a "KLH-conjugated polypeptide CMTRPIKGPRDIQLDLE
MITVN, which corresponds to amino acids 406-426 of mouse and rat DANCE protein" (page 22477, column 1).

In addition, as set forth in *In re Marzocchi*, 169 USPQ 367, 369 (CCPA 1971):

> The first paragraph of § 112 requires nothing more than objective enablement. How such a teaching is set forth, either by the use of illustrative examples or by broad terminology, is of no importance.
>
> As a matter of Patent Office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the

> subject matter sought to be patented *must* be taken as in compliance with the enabling requirement of the first paragraph of § 112 *unless* there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

Contrary to the standard set forth in *Marzocchi*, the Office Action has failed to provide any ***reasons*** why one would doubt that the guidance provided by the present Specification would enable one to make and use the recited variants, biologically active and immunogenic fragments of SEQ ID NO:1. Hence, a *prima facie* case for non-enablement has not been established with respect to the recited variants, biologically active and immunogenic fragments of SEQ ID NO:1.

Accordingly, for all the above reasons, the claimed subject matter is described in the Specification in such a way that one skilled in the art can make and/or use the claimed invention. Therefore, reconsideration and withdrawal of this rejection to the claims are respectfully requested.

CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding rejections. Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact Applicants' Attorney at (650) 845-5415.

Please charge Deposit Account No. **09-0108** in the amount of **$ 110.00** as set forth in the enclosed fee transmittal letter. If the USPTO determines that an additional fee is necessary, please charge any required fee to Deposit Account No. **09-0108.**

Respectfully submitted,

INCYTE GENOMICS, INC.

Date: December 11, 2002

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Attachment Nakamura, T. *et al.* reference

VERSION WITH MARKINGS TO SHOW CHANGES MADE IN THE CLAIMS

Claim 41 has been amended as follows:

41. (Once Amended) An isolated polypeptide selected from the group consisting of:

a) a polypeptide comprising an amino acid sequence of SEQ ID NO:1,

b) a polypeptide comprising a naturally occurring amino acid sequence at least [85]90% identical to an amino acid sequence of SEQ ID NO:1, said polypeptide having extracellular matrix protein activity,

c) a biologically active fragment of a polypeptide having an amino acid sequence of SEQ ID NO:1, said fragment having extracellular matrix protein activity, and

d) an immunogenic fragment of a polypeptide [having] consisting of at least 5 amino acids of the [an] amino acid sequence of SEQ ID NO:1.